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Fertility Flash™

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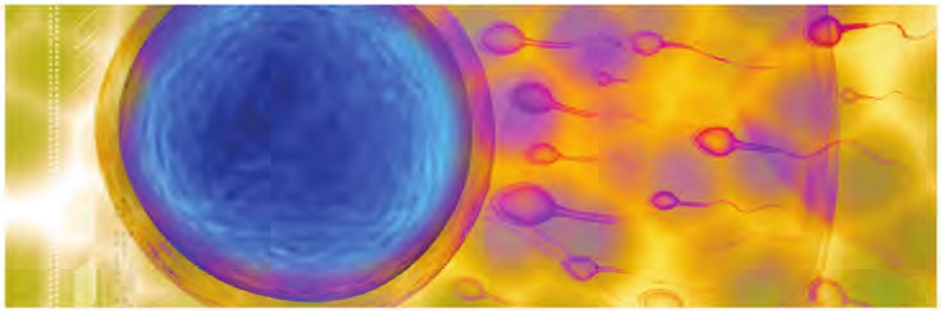

Upcoming Events and Seminars at PFC

EVENTS & SEMINARS

OVERCOMING INFERTILITY: THE NEXT STEP TO PARENTHOOD
Wednesday, March 29th
Thursday, May 18th
Visit www.pacificfertilitycenter.com/events

FERTILITY PRESERVATION WEBINAR
Thursday, March 16th
Thursday, May 25th
Visit www.pacificfertilitycenter.com/events

Location:
Pacific Fertility Center
55 Francisco Street, Fifth Floor
San Francisco, CA 94133

MIND/BODY @ PFC
Saturday, March 11th
Visit www.pacificfertilitycenter.com/mb
for more information and to register online

Fertility Preservation of Embryos (FPe) — SCIENCE PULSE

Fertility Preservation of Embryos (FPe)

A couple consulted with me recently about their plans for their family. In their mid-30s, they were committed to each other, and to building a family, but deeply involved in a family startup business. They had decided that family building would have to wait for 5 years until they could provide the time and energy that children would require. We talked about Fertility Preservation of Embryos (FPe) as a way to protect their future option for pregnancy.

FPe is an extraordinarily effective technique at Pacific Fertility Center. Couples that want to build a family sometime in the future, or any woman that is willing to commit to a sperm source, can save healthy embryos and achieve high pregnancy rates 5 or 10 years later. Embryos that are chromosomally normal, preserved today, offer high pregnancy rates for many years into the future.

A chromosomally normal embryo, known as a euploid embryo, transferred into a healthy uterus, will produce a pregnancy 2 out of 3 times, about 65%. 3 healthy embryos each with a 65% implantation rate, offer the potential, on average, of 2 healthy children (3 * 0.65 = 1.95, or about 2). These pregnancies carry a high implantation rate, with low miscarriage risk, and the embryos are pre-screened for chromosome abnormalities such as Down Syndrome.

FP of embryos works like this: Eggs are retrieved from the ovaries with conventional in vitro fertilization techniques. Sperm is added to the eggs in the lab and resulting embryos are incubated for 5-7 days to the blastocyst stage. A few cells are culled from the embryo to count chromosomes. Euploid embryos are cryopreserved.

At a future date, one euploid embryo is warmed from the batch and transferred to the mother. Pregnancy rates are high, and since only one embryo is transferred the risk of multiple gestation is quite low.

This couple went ahead with FPe. They produced 15 eggs, 10 of which fertilized to produce embryos. Embryos were cultured for 5 or 6 days to the blastocyst stage. On testing, 3 of the embryo showed normal chromosomes.

Those 3 chromosomally normal embryos offer an excellent potential for pregnancy, and the couple feel secure that they have protected their family-building for the future.

— Philip Chenette, M.D.
PFC Physician

Security in the Laboratory — FROM US TO YOU

Security in the Laboratory

We read with sadness of the recent case in Holland where it appears as though the oocytes belonging to some patients were inseminated with the wrong sperm. The University of Utrecht announced in December that up to 26 couples may be affected and that an investigation is ongoing. Although it's likely that those of us outside this investigation may never find out what happened, we still need to learn what we can from the incident. Early reports suggest that sperm from one man may have remained in an injection needle, or needle holder, when the laboratory staff moved on to inseminate the oocytes from another couple. This situation persisted as subsequent patients had their oocytes injected with sperm.

All of us in the IVF laboratory take great pride in our work and every attempt is made to set up a system that cannot allow mixing of sperm and eggs between couples. This system is scrutinized internally and by our accrediting agencies during routine inspections with the intention that it should be designed to prevent mistakes entirely. We of course feel that a mistake of this nature cannot happen, but yet we are always looking for ways to make the system even more foolproof. And sometimes, reading about the mistakes of others can be an important part of the process. We always ask, "Could that happen here?"

In this particular case, the answer is a definitive "no". Our injection procedure is very explicit in requiring a complete change of needle between patients, and also in preventing the needle holder from ever getting touched by any biological material. Unlike practices elsewhere, we have decided that no embryologist at PFC will ever backload a needle with sperm, and instead will work with just one egg and one sperm at a time. Sure, this takes longer, but it's much safer and prevents any possibility of cross contamination. After we complete a procedure, the microscope and needle holders are stripped down and cleaned before another procedure can be started. And all procedures are witnessed and performed by 2 embryologists as an extra layer of protection. There's always a second set of eyes on these critical procedures because we don't want to expose our patients to any risk.

Security measures are everywhere in the IVF laboratory because this is a place where mistakes should not happen. But, we also value the integrity and honesty of our embryologists and I know that if anyone was to make a mistake, they would tell me immediately. One of the first things that new embryologists learn here is that any mistake must be reported as soon as possible and that they will not be fired for owning up to a mistake. This is important, because the sooner a mistake is discovered, the fewer consequences there will be. There was an infamous case a few years ago where a physician in another IVF program knew that he had made a mistake and transferred the wrong embryo to a patient. I have new embryologists study that case because that physician decided to keep the mistake a secret and when it was eventually discovered 2 years later multiple lives and careers were ruined. If that individual had owned up to the mistake immediately, 99% of that damage could have been prevented. Reading the court transcript from that case is sobering for a new embryologist, but it really drives home the importance of honesty and integrity.

We take great pride in our work and if there's ever a time where we think we could have done better, we will always disclose this information to our patients. We feel good about the culture that we have developed here and we trust the system we have in place for error prevention. It's an important part of what we do, who we are, and it allows us to go home to our families at night knowing that our work was done well.

— Joe Conaghan, PhD
PFC Laboratory Director

Long-term storage of oocytes, sperm and embryos — FROM US TO YOU

Long-term storage of oocytes, sperm and embryos

Pacific Fertility Center maintains a sizeable "Tissue Bank" (TB) where we hold oocytes, sperm and embryos in long-term frozen storage for our patients. Since PFC has existed in San Francisco for almost 30 years, we do have some tissues that date back to the late 1980's. But the vast majority of the frozen samples are from the last 5 years as patients usually do not intend to store for very long periods of time. Patients that freeze sperm usually intend to use it imminently. In fact PFC does not charge a storage fee for sperm samples that we maintain for less than 3 months. Patients using samples from a sperm bank will often hoard several samples from their favorite donor in case that they want a 2nd child in a few years using that same sperm, or if the stock of a certain donor is running low at the sperm bank. The sperm bank will also reserve and hold sperm for patients, and will "buy back" unused sperm if they have been storing it.

Embryo storage too should be a short-term option for patients as most patients freezing embryos are trying to get pregnant as soon as possible, and then looking to have subsequent pregnancies as soon as is practical after giving birth. Nowadays, with the easy availability of oocyte freezing, we don't see too many patients tucking away frozen embryos for 10 or 15 years. What we do see however, is patients struggling to discard embryos after their fertility treatment is completed. This situation arises as many IVF cycles yield more embryos than a patient can use, and the embryos remaining in frozen storage are costly to maintain. PFC reaches out to patients once a year on the anniversary of the freeze month to give patients options on the further storage, use or disposition of the embryos. The options include continuing to store the embryos, donate the embryos to research or have the embryos discarded by PFC. Some patients struggle with these choices, especially if they have already completed their family. The decision to discard embryos that are genetic siblings to their children is a tough one. Often these patients will continue storing the embryos indefinitely as they cannot commit to discarding or donating to research. PFC currently charges $600 per year to keep embryos stored, so indecision costs are high.

Patients that are coming to PFC for oocyte freezing really are looking at long term storage most of the time. Women who decide to delay having a baby for career or other reasons are usually thinking of storage for 5 years or more, and young women in their 20's could be storing their eggs for considerably longer. So although historically we've considered ourselves a short-term storage facility, this is changing rapidly as more and more women store oocytes.

This year we are expanding our storage area in the PFC facility and making several upgrades in security and safety. Most of our stored tissues will be moved to a special facility in our building where we are in the final stages of building a state of the art facility. Since all frozen tissue is stored in liquid nitrogen at almost minus 200 degrees Celsius (-321ºF) there are local and State regulations that come into play for building out a new storage facility of the size we need. In addition we are installing a multi-level security system that requires 3 levels of authentication for entry, 24-hour video surveillance, dual alarm systems and brand new storage tanks. The tanks themselves are very low maintenance and are really like giant thermos flasks on wheels. Each tank is secured against movement in case of an earthquake, connected to a liquid nitrogen reservoir and has a small onboard monitoring computer. Other than for running the computer the tank does not need electricity and the liquid nitrogen can be topped up manually at any time by an embryologist. However, the computer is monitoring and maintaining the liquid levels most of the time in the same way that the autopilot on an airplane does most of the flying. The computer will alert us if there is a problem or a power failure. The automated phone based alarm system calls the on-call embryologist for physical inspection before the alarm can be shut off. The tanks have a 2-week internal reservoir for liquid nitrogen as well as a connection to the bulk supply. Furthermore, we conduct a manual inspection of the tanks at the end of each day, 7 days a week, to ensure that everything is in full working order. The alarm system and the back-up power generator are each tested in a frequent and periodic manner.

The frozen tissues at PFC are housed in a stable, safe and modern environment with continuous monitoring and upkeep. As far as we know, there is no limit to how long cells remain viable in the frozen state. We have had some patients return to thaw embryos after more than 10 years and the embryos were no different that when they were frozen. The temperature of liquid nitrogen is so cold that scientists think that all biological activity is stopped and that there are no issues with very long term storage. But for most patients, shorter tem storage should be the goal. We are happy to counsel patients on their options for storage or disposition of their frozen biological tissue and help them make the appropriate decisions for their family.

— Joe Conaghan, PhD
PFC Laboratory Director

Brief Rest after IUI Brings No Benefit — IN THE NEWS

Brief Rest after IUI Brings No Benefit

In an attempt to improve pregnancy rates, doctors often ask women to lie still for a brief period after intrauterine insemination (IUI). But does this really help? A large single-center randomized controlled trial suggests that it doesn't. The study contradicts findings from previous smaller studies—one of which was based on just one treatment cycle, rather than the more likely scenario of multiple cycles.[1]

By contrast, the Amsterdam study looked at 479 patients undergoing 1,934 IUI cycles. The researchers randomized patients with mild male subfertility or an unknown cause of infertility (idiopathic) to either lie still for 15 minutes after IUI (950 cycles) or to move around right away (984 cycles). The cumulative ongoing pregnancy rate per couple was actually lower in the immobilization group (32.2 percent) than in the mobilization group (40.3 percent)—although this difference was not considered statistically significant.

The researchers presented their findings at this year's annual meeting of the European Society of Human Reproduction and Embryology (ESHRE). They say the findings are strong enough to make bed rest recommendations obsolete.

1. MDedge.com: Study shows no benefit with brief immobilization after IUI.

Get To Know Our Embryologist Jin

Looking back at my life's road, I feel really blessed to have been born into my particular family. Both of my parents are academic professors at a university in northeast China. From childhood, they encouraged me to act with integrity, prudence, and meticulousness. My parents have always done their best to support me in every possible way. Without them, I wouldn't be the person I am today.

I finished my college education in China, majoring in biotechnology, biochemistry and molecular biology. After graduation I decided to continue my studies in Australia and in 2005 I started my master's in biology in an entirely new environment at the University of Newcastle.

Being far from home was not easy for me at first. I was lucky though, to have a great mentor, Laureate Professor John Aitken. John is a pioneer in male reproduction and is a well-known reproductive biologist in Australia and around the world. He patented the world's first chemical contraceptive which kills sperm as well as bacteria causing sexually transmitted infections. My co-supervisor Dr. Brett Nixon is knowledgeable, supportive, and patient. I gained from John and Brett not only professional knowledge, but also scientific ways of thinking and working.

At the University of Newcastle I was introduced to the field of reproductive biology. I was investigating whether an enzyme called "NADPH oxidase" is present in sperm. It was so interesting seeing sperm swimming under the microscope for the first time; they were super active, especially as they got ready for fertilization. The time that I spent in the Aitken lab was an amazing experience. As I was finishing my master's degree I became more interested in biology, especially reproductive and developmental biology.

Upon finishing my master's degree, I moved to Sydney for my PhD at the University of New South Wales. I was drawn to Sydney by the opportunity to study human embryonic stem cells; interesting pluripotent cells that can differentiate into any cell type in a human body. I was among the first people reporting applications of a combined epigenetic and non-genetic approach for reprogramming human somatic cells and the trans-differentiation ability of the reprogrammed cells. This was a big step toward the potential clinical application of stem cell-based therapy. I published some good papers on my project and won the award for the best publication of the year at UNSW.

However, embryonic stem cells seemed to upset me a little bit – they don't swim and they don't change much. They proliferate and differentiate, but all you can see is that you have more cells in a petri dish the next day. I wanted to go back to germ cells and reproductive biology. So, when I had the opportunity to interview with Professor Renee Reijo Pera, an expert in reproductive biology and stem cell biology at Stanford University, I was thrilled.

In 2010 I moved to California as a postdoctoral fellow in the Institute for Stem Cell Biology and Regenerative Medicine. Renee served as the Director of the Center for Human Embryonic Stem Cell Research and Education, and the Center for Reproductive and Stem Cell Biology. During the first year in the Reijo Pera lab, I still focused on embryonic stem cells and tried to differentiate them into sperm. Then one day Renee showed me a movie she saved from a previous study, where she and her postdoc monitored human embryo development from day 1 to day 5. I was amazed by how much one little cell can do and how lives all begin from these single cells. I told Renee right away that I wanted to have a project studying embryo development. Thus, I started my journey working with human embryos in 2011.

At Stanford, I was exposed to one of the most active and technologically advanced academic environments, and was able to collaborate with some of the most intelligent people in the world. As a result of our studies of early cell divisions in the embryo, a device was designed to predict the developmental potential of an embryo on day 1 (right after fertilization), rather than day 3 which is more traditional and somewhat subjective. By using a video time-lapse monitoring system, the potential of each embryo could be predicted reliably, and early in the process. This new technology holds great promise for improving IVF success rates because it enables embryologists to better select an embryo for transfer from among a group of embryos belonging to a single patient. It may also significantly lower IVF costs. Information about this invention was published in Nature Communications earlier last year[1].

When I finished my fellowship at Stanford and was facing career choices, I realized that I didn't want to be a scientist in a research laboratory for the rest of my life. Instead, I was eager to be more involved in applying new concepts and technologies to help people directly. So in 2016, I accepted a job offer and started to work at PFC. My experience thawing human embryos donated for research, culturing them in the time-lapse incubator, and manipulating them for all sorts of analyses was a great foundation for training as a clinical embryologist.

It has been a short year for me at PFC, as the time has passed quickly as I applied myself to learning all aspects of the job. I have had the good fortune to experience world-class expertise, as well as high standards in clinical care and treatment. I am really proud to work with our physicians who are professional, knowledgeable and caring, and the team of embryologists and clinical staff, who are sincere and responsible.

My next goal is to combine my research background with my clinical experience to help each and every couple that comes to PFC to create their dream family. I hope that IVF will one day become simpler with more automated technologies to help lower costs but increases success. We continue to seek a better understanding of embryos; how they develop, why they sometimes fail and how we can create a better laboratory environment. This process never ends as we can always do better, and as we grow, so do the embryos.

1. L. Yanez*, J. Han*, B. B. Behr, R. A. Reijo Pera, D. Camarillo, Human oocyte developmental potential is predicted by mechanical properties within hours after fertilization. Nat Commun. 2016; 7: 10809

Get To Know Caitrin, Our New Director of Operations

To this day, my mom tells a story about a call she got from my teacher when I was in preschool. Like many of my classmates, I had gotten in the habit of bringing a doll to school. Unlike those same classmates who spent recess futzing with their doll's attire or untangling hair, I marched around the playground, my teacher said, introducing her as "my premature baby". Now that I understand the clinical connotations of that statement, the story makes me cringe. I tell it because it helps explain why I chose to join PFC in 2016: I have always been fascinated by babies, pregnancy and birth.

In fact, my first 'internship' was shadowing a Labor and Delivery Nurse in my hometown of Madison, Wisconsin. For reasons still unfathomable to me, a number of women and men allowed a slack-jawed high schooler to observe the moment they became a family. I remember being struck by two things: (1) how profound it was to be part of the team in the room, helping and encouraging the parents-to-be, and (2) that it was a far harder, messier experience than I anticipated. As Director of Operations, I am rarely in the room with our patients. I like to think, though, that the work I do managing process improvements in the clinic both gives me a spot on the proverbial 'team', and makes the arguably harder, messier experience of getting pregnant less so.

It is immensely gratifying to apply the healthcare service design skills I've honed over the past decade – first as a management consultant, then as a Stanford business school student, and finally as Director of Operations for a Google-backed telemedicine company – towards the goal of making babies (and by extension, families!). While my husband and I currently only call ourselves parents to our bully mix Tater Tot, part of my deep attachment to PFC stems from seeing the impact of fertility treatments up close. Of the six babies born in my extended family over the past year (it was a 'productive' 12 months!), half were through IVF. I also have a growing number of friends who have frozen their eggs as a mechanism to ensure they have the mental and biological space to make clear-eyed decisions about their partner and career.

This is all to say: I am proud of what we make possible at PFC, whether it be a family now, or options later. I'm grateful to the patients and team members who've made that degree of personal and professional satisfaction possible for me.

CHECK OUT OUR NEW INSTRUCTIONAL LAB VIDEOS

We are excited to announce that we have created 3 new lab instructional videos on our website!

We created these informational videos to provide easy-to-reference information for our patients who are interested in learning more about egg fertilization and day 3 and day 5 embryo development. PFC's Laboratory Director, Dr. Joe Conaghan, takes you into the lab and under the microscope to learn and see the process of egg fertilization, embryo development at day 3 and again at day 5.

To view the videos, select the "Current Patients" tab on the PFC homepage and select "Lab Instructional Videos" under "Patient Resources."

GET TO KNOW THE PFC PHYSICIANS

Did you know you can watch a short personal video about each of our physicians and lab director?

The PFC physicians took the time to record personal videos about why they chose to go into fertility medicine and become IVF physicians.

Get to know them by watching their personal videos on our website. Visit *www.pacificfertilitycenter.com/fertility-specialists* and choose the physician video you would like to watch.